REMARKS

Claims 1-16, 25, 39, and 40 are withdrawn as being part of a non-elected invention, and Claims 17-24, 27-29, 31, 33, 37-38 are under Examination.

Applicants have amended Claims 17-20, 24, and 37 herein. Claims 26, 30, 32, and 34-36 have been cancelled.

Support for the amendments is found throughout the present specification. Further, the addition of the phrase "electroporating the muscle tissue" can be found, inter alia, in paragraphs [0136] – [0143]; and the addition of phrase "wherein the biological equivalent is stimulating angiogenesis" and "retains the function of stimulating angiogenesis in the muscle tissue of the subject" (Claims 17 and 19, respectively, for example) can be found, inter alia, in Example 4 and paragraphs [0059], [0169], and [0172]; and the addition of phrase "retains a myogenic promoter activity" in Claim 18 can be found, inter alia, in Example 2 including paragraph [0149]. Thus, no new matter is added.

The objections to Claims 34-36 are rendered moot due to the cancellation of same.

The Applicants have amended the specification to replace the term MyoD in lines 1-3 of paragraph [0162] with the term "myogenin", which is consistent with the prior made amendment (in December 4, 2006 Response). Applicants submit that the entire paragraph [0162] refers to an experiment detecting myogenin levels in a treated muscle, the results of which are shown in Figure 6, which is labeled "Induction of Myogenin in Skeletal Muscle by IGF-I (3'GH) Plasmid Therapy." This amendment finds further support in the brief description of Figure 6 in paragraph [0036]. This correction does not constitute new subject matter because the title and brief description of Figure 6 is consistent with the amendment.

I. Claim Rejections 35 U.S.C. § 112, Enablement:

Claims 17-24, 26-38 were rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. Applicants respectfully traverse based on the amendments made herein and the arguments below.

The Examiner has acknowledged that the specification enables methods for stimulating angiogenesis in a subject comprising: injecting into a muscle tissue of the subject an isolated nucleic acid expression construct, wherein the muscle tissue comprises cells, wherein the isolated nucleic acid expression construct comprises: a myogenic promoter, a nucleic acid sequence encoding IGF-I and a 3'UTR, wherein the isolated nucleic acid expression construct is substantially free from a viral backbone; the myogenic promoter, the nucleic acid sequence encoding IGF-I and 3'UTR are operably linked, thereby delivering to the cells of the muscle tissue of the subject the isolated nucleic acid expression construct, thereby expressing said encoded IGF-I in said cells and thereby stimulating angiogenesis in the muscle of said subject. The present claims as amended are directed to such methods.

The present claims do not recite "any nucleic acid sequence encoding any fragments of IGF-I," (See Page 4 of Office Action) but rather recite "a nucleic acid sequence encoding an insulin-like growth factor I ("IGF-I") or functional biological equivalent thereof, wherein the functional biological equivalent is **stimulating angiogenesis**" (Claim 17). The Applicants do not attempt to seek claims that would cover **any** fragments. Instead, the Applicants direct claims to cover the sequences that encode IGF-I or a functional biological equivalent that is stimulating angiogenesis. The specification, and in particular Example 4, detail methods for determining angiogenic activity.

Furthermore, the present claims do not recite "any fragment of a myogenic promoter," (See Page 4 of Office Action) but rather recite "a myogenic promoter" (Claim 17).

Accordingly, it is respectfully submitted that the current specification provides an enabling disclosure for the claimed invention and, thus, the present rejection should be withdrawn.

II. Claim Rejections 35 U.S.C. § 112, Written Description:

The Examiner has rejected Claims 17-24 and 27-28 on the basis that they do not comply with the written description requirement of 35 U.S.C. §112, stating that the claims contain material which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. The Applicants respectfully traverse.

The Applicants refer to the arguments supporting an enabling disclosure, above, to partly support the Applicants' arguments that the present specification provides written description support for the claimed invention.

Furthermore, the specification describes in detail the characteristics of the claimed invention (Claim 17 being representative), which includes the element "a nucleic acid sequence encoding IGF-1, or a functional biological equivalent thereof, wherein the functional biological equivalent is stimulating angiogenesis." As mentioned in the remarks, above, the specification clearly discloses this element in, *inter alia*, Example 4 and paragraphs 59, 169, and 172.

Moreover, the specification teaches the limitations of Claim 20, which recites that the IGF-I or functional biological equivalent thereof "has an amino acid sequence of SEQ ID NO: 4 or SEQ ID NO: 4 with conservative amino acid substitutions and retains the function of inducing angiogenesis in the tissue of a subject." This is described in paragraph [0147] as discussed above, which specifically teaches SEQ ID NO: 4 with or without conservative amino acid substitutions, and lists the stimulation of angiogenesis in a subject as a biological activity of IGF-I.

The specification teaches the limitations of Claim 37, which recites "wherein the encoded IGF-1 is a biologically active polypeptide that has been engineered to contain a distinct amino acid sequence while simultaneously having similar or improved biological activity when compared to the IGF-I polypeptide." As discussed above, the specification describes in paragraph [0147] that a polypeptide could be engineered to contain distinct amino acid sequences while having similar or improved biological activity compared to IGF-I. The specification goes on to describe in [0147] that

one example of a biological activity of IGF-I which could be similar or improved is the stimulation of angiogenesis in a subject.

Applicants respectfully submit that the limitations and descriptions of the claimed invention are described wholly and in detail in the specification as filed. It would therefore be readily apparent to one of skill in the art upon reading the specification that the inventor was in possession of the invention at the time of filing.

III. Claim Rejections 35 U.S.C. § 112, second paragraph:

Claims 18-21 and 24 are newly rejected on the grounds of being indefinite. The Examiner states that, as a result of previous amendments, these claims recites "further comprising selecting", which is unclear.

In response, Applicants have amended Claim 17 to recite "...comprising the steps of:" rather than "...comprising:", for the sake of clarity.

Applicants have amended Claims 18-21 and 24 to remove the phrase "further comprising the step of selecting...", and have corrected grammatical inconsistencies in each of these claims.

Applicants submit that Claims 18-21 and 24, as amended, are definite, and are therefore in condition for allowance.

IV. Claim Rejections 35 U.S.C. § 102:

The Examiner has rejected Claims 17, 19-21, and 31-38 under 35 U.S.C. § 102 as being anticipated by Alila et al. *Hum. Gene Therapy* 8:1785-1795, 1997 ("the Alila Reference"). The Applicants respectfully traverse..

The Applicants have amended the claims to specify that the isolated nucleic acid construct is delivered using electroporation. This technique is novel and distinct from the delivery method taught in the Alila Reference, which relies on simple injection. Support for this amendment can be found in [0094], [0098], [0100], [0108], Section XII, and Example 4.

The Applicants respectfully submit that, in light of these amendments, the Alila Reference fails to anticipate the claimed invention; therefore this rejection should be withdrawn.

VII. Claim Rejections 35 U.S.C. §103(a):

A. The Examiner has rejected Claims 22-23 under 35 U.S.C. §103(a), as being unpatentable over the Alila Reference in view of van Deutekom et al. *Mol. Med. Today*, 214-220, 1998 ("the van Deutekom Reference"). The Applicants respectfully traverse.

The Applicants respectfully submit that Claims 22-23 are not rendered obvious by the cited references, alone or in combination. Specifically, the current claims recite the use of electroporation of the muscle tissue in order to facilitate delivery of the nucleic acid expression construct. This element is not taught or suggested in any of the cited references, and therefore none of these references, alone or in combination, renders the current invention obvious. Accordingly, it is respectfully requested that this rejection be withdrawn.

B. The Examiner has further rejected Claims 18, 24, and 26-30 under 35 U.S.C. §103(a) as being obvious over the Alila Reference in view of the Draghia-Akli Reference (cited previously), the Fewell Reference (cited previously) and the Isner Reference (cited previously). The Applicants respectfully traverse.

The suggestion to combine references must be from the prior art, not Applicants' disclosure. See Section 2143 of the M.P.E.P., which states: "The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)."

The Applicants respectfully submit that the combination of the cited references is not proper for purposes of rendering the claimed invention obvious. The Alila Reference is silent with regard to using electroporation as a means of delivery. While intramuscular electroporation is discussed in the Fewell and Draghia-Akli References, it relates to delivering a plasmid to increase systemic levels

of human factor IX in the case of Fewell, and delivering a plasmid to ectopically express a porcine growth hormone releasing hormone in the case of Draghia-Akli.

In contrast, the present invention requires a plasmid which is capable of expressing IGF-I or a functional biological equivalent thereof for **stimulating angiogenesis**. The combination of cited references are absent such teaching, thus there is no motivation to combine or, if combined, the teaching still fails to render the claimed invention obvious.

Accordingly, the Applicants respectfully submit that the cited references, alone or in combination, fail to render the claimed invention obvious and the instant rejection should be withdrawn.

VIII. Conclusion

The Applicants respectfully submit that, in light of the foregoing comments and amendments, all pending claims are now in condition for allowance. A Notice of Allowance is therefore requested.

If the Examiner has any other matters which pertain to this Application, the Examiner is encouraged to contact the undersigned to resolve these matters by Examiner's Amendment where possible.

Respectfully submitted,

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